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Octreotide in the Treatment of Bleeding Due to Angiodysplasia of the Small Intestine

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Three patients with a history of bleeding due to small bowel angiodysplasia (repeated melena or occult fecal blood with serious anemia) were treated for 10–40 months with octreotide, a somatostatin analog that reduces the splanchnic flow. A dose of 0.1 mg subcutaneously twice a day was followed by an increase in hemoglobin, and reduction or elimination of the need for transfusions. There were no further melena episodes, and stool hemoglobin became stably negative in two cases. Suspension of the drug after 6 months in one case was followed by renewed bleeding, and resumption led to a further response. Lower doses tried in another case were ineffective. Although these uncontrolled clinical cases do not prove its efficacy, octreotide appears to be beneficial in the control and prevention of bleeding due to diffuse small bowel angiodysplasia. There is no evidence that it results in regression of angiodysplasias, as they persisted in the patient subjected to control jejunoileoscopy.

INTRODUCTION

Small bowel angiodysplasia is still a problematic entity. Its incidence is uncertain, since it is not readily detected and may remain clinically silent (1). Even so, it is probably responsible for up to 24% of upper gastrointestinal (GI) bleeding regarded as of obscure origin when first assessed (1, 2). Once identified invasively by superior mesenteric arteriography or intraoperative enteroscopy, its recognition is now made easier by jejunoileoscopy, which also enables therapeutic procedures such as electrocoagulation to be performed (3–6). Optimum management of small bowel angiodysplasia, however, is still an open question. Resection of the segments involved or suture of individual lesions under intraoperative enteroscopic control (via direct vision and transillumination) have given satisfactory results (7). Yet, both surgery and electrocoagulation are difficult to apply when treating multiple and usually extensive lesions (8–10). Medical management, too, is far from being standardized. Some authors have indicated that estrogen-progesterone therapy diminishes bleeding from GI angiodysplasia (11–13). In a controlled study, however, hormonal therapy was not effective in decreasing bleeding from small bowel angiodysplasia (14). Octreotide acetate (a synthetic somatostatin analog) reduces the splanchnic flow and has thus been proposed for the control of GI bleeding (15, 16). It could therefore be indicated in the treatment of bleeding due to angiodysplasia not open to surgical or endoscopic management. Only one paper has so far been published with respect to the small intestine (17). It has thus been thought useful to present our results in an open trial of octreotide in three patients.

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MATERIALS AND METHODS

Three women aged 17–74 yr were studied (clinical background in Table 1). Patients I and II presented chronic occult enteric bleeding with anemia lasting 2 yr, and 6 months, respectively. Patient III had a history of repeated melena episodes with serious anemia lasting more than 2 yr, and also suffered from anti-HCV-positive liver cirrhosis. She was free from esophageal/gastric varices and congestive gastropathy, and her coagulation parameters were normal. All patients had received repeated blood transfusions (mean in Table 2).

Diffuse small bowel angiodysplasia in segments ranging from 40 to 80 cm beyond the ligament of Treitz was diagnosed by jejunoileoscopy with a push-type (XSIF-10LY) or a sonde type (SIF-SWIV) prototype (Olympus Optical Corporation Europe GMBH, Hamburg) in two cases and one case, respectively. There was no active bleeding at the time of the examination. In one case, ^{99}Tc-erythrocyte scintiscan had shown jejunoileal accumulation. Before jejunoileoscopy, all patients had been repeatedly examined in various ways, including esophagogastroduodenoscopy, total colonoscopy (also performed during bleeding in the patient with recurrent melena), and small intestine enema. Other possible sources of bleeding had been ruled out in patient III. Angiodysplasia of the right colon had been found in patient I, and of the ascending, transverse and sigmoid colon in patient II. Regression of these lesions achieved by hot biopsy electrocoagulation, and endoscopically confirmed at follow-up, had not re-

TABLE 1
Clinical Backgrounds

Patient	Age (yr)	Symptoms	Duration before Diagnosis	Angiodysplasia in Other Sites	Concomitant Diseases
I	17	Anemia, FOBT+*	24	Right colon	
II	64	Anemia, FOBT+	6	Right transverse sigmoid colon	
III	74	Melena, anemia	24		Liver cirrhosis

* FOBT+ = fecal occult blood test, positive.

TABLE 2
Hemoglobin levels (Hb), FOBT, and Transfusion Requirements (mean red cells units per month) in Patients Before and During Octreotide Management

Patient	Before Treatment			During Treatment			
	FOBT*	Hb	Red cell units/mo	Follow-up (mo)	FOBT	Hb	Red cell units/mo
I	+	6	3	40	−/+	11	0.5
II	+	5.5	4	12	−	13	0
III	Melena	8	4	10	−/+	11	1

* FOBT = fecal occult blood test: −/+ = seldom positive.

solved the GI bleeding, and the possibility of concomitant small intestine angiodysplasia had been investigated. Coagulation diseases were ruled out in all cases.

The magnitude and extent of the small intestine lesions prevented surgical or endoscopic management. Octreotide (O.1 mg subcutaneously twice a day) was administered in cases II and III, whereas this dose was reached progressively from 0.05 mg once a day, and then twice a day, in case I. All patients were examined after 15 days and 30 days, and then monthly in the absence of other clinical requirements. Transfusions (1–2 units) were given during the follow-up when hemoglobin (Hb) values fell by more than 2 g/100 ml, or below the threshold of 8 g/100 ml.

The following data were collected on inclusion in the study and during follow-up: melena episodes, routine blood values (particularly Hb, glucose, amylase), and occult fecal blood.

The response to treatment was assessed with reference to mean red cell units transfused per month, Hb levels, melena, and occult fecal blood. Side effects (diarrhea, glucose intolerance) also were noted. A control jejunoileoscopy with the push type instrument was performed in patient II only.

RESULTS

Patients have so far been treated for 10–40 months. Hb levels, transfusion requirements, and fecal blood are illustrated in Table 1. Hb levels increased and transfusion requirements decreased in all patients during treatment (Table 2). A rise or stabilization of Hb levels, plus a reduction or elimination of the need for transfusion, was apparent in the first month of treatment with 0.1 mg twice a day only (patient II and III). Patient I has not required transfusions for the last 8 months, her Hb is stable at about 11 g/100 ml, and no occult fecal blood has been detected (Fig. 1). For patient II, an attempt to suspend the drug after 6 months was followed by anemia and the reappearance of occult blood. Resumption was followed by a further response in the form of stable Hb, and no transfusions have been required during the last 6 months (Fig. 2). Patient III, on the other hand, although free from melena, has occasionally been stool Hb positive and has continued to require an average of one transfusion unit per month (Fig. 3).

There have been no instances of diarrhea or steatorrhea. Fasting and post-prandial blood glucose values have not altered, and there has been no increase in serum amylase. There have been no variations in the values of parameters indicative of liver and kidney function.

Control jejunoileoscopy performed in patient II after 12 months showed non-bleeding small bowel angiodysplasia. Patients I and III refused further endoscopies.

DISCUSSION

Our findings suggest that octreotide may ameliorate bleeding in some patients with diffuse and otherwise refractory small bowel angiodysplasias. The lesions observed in these three cases were not open to surgical or endoscopic management on account of their extent and site, whereas colonic angiodysplasias in two patients had been readily resolved by electrocoagulation. As in the only other case in the literature (17), octreotide was followed by reduction or regression of occult fecal blood and cessation of recurrent melena, accompanied by reduction or elimination of the need for transfusions.

It should not be forgotten, however, that small bowel angiodysplasia may stop spontaneously despite a long bleeding history (2, 14).

Torsoli *et al.* (17) achieved a positive effect with 0.05 mg twice a day. In our experience, however, this dose

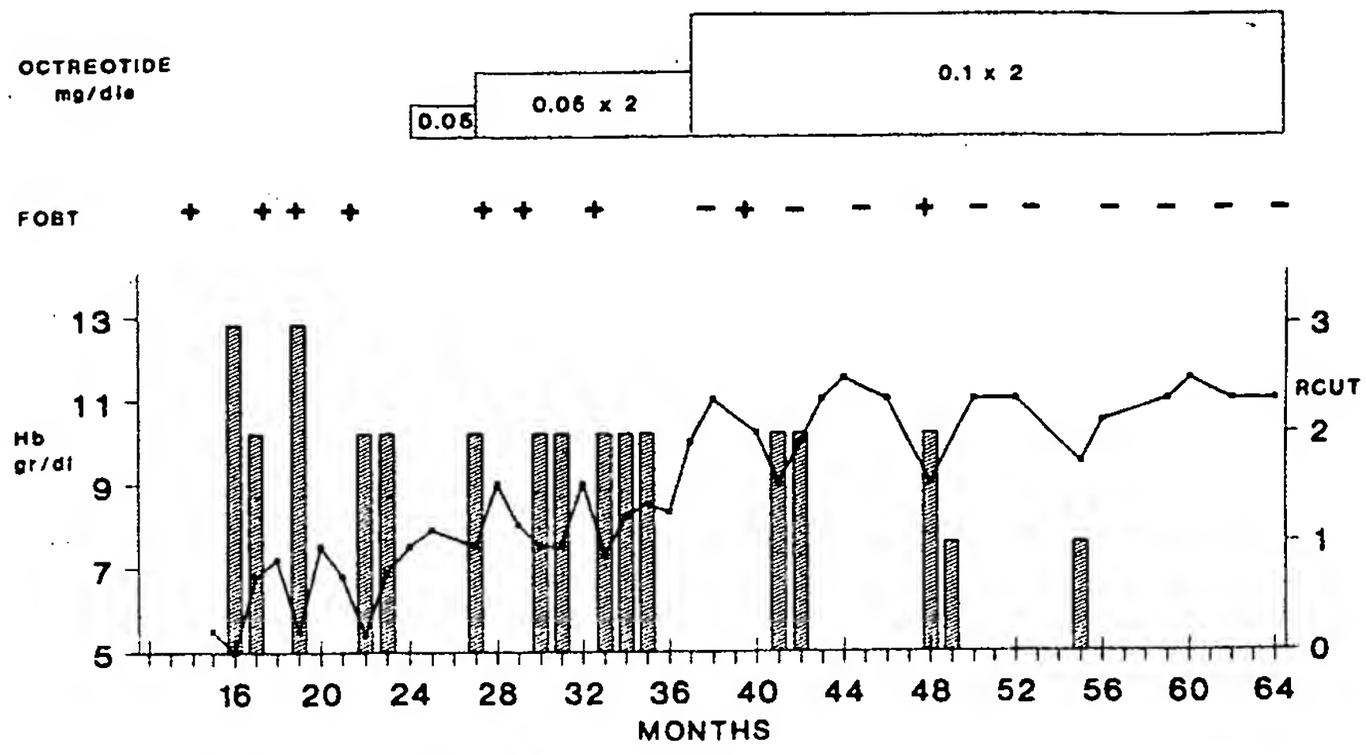

FIG. 1. Hb levels, fecal occult blood test *(FOBT)*, and number of red cell units transfused *(RCUT)* in relation to the treatment of patient I.

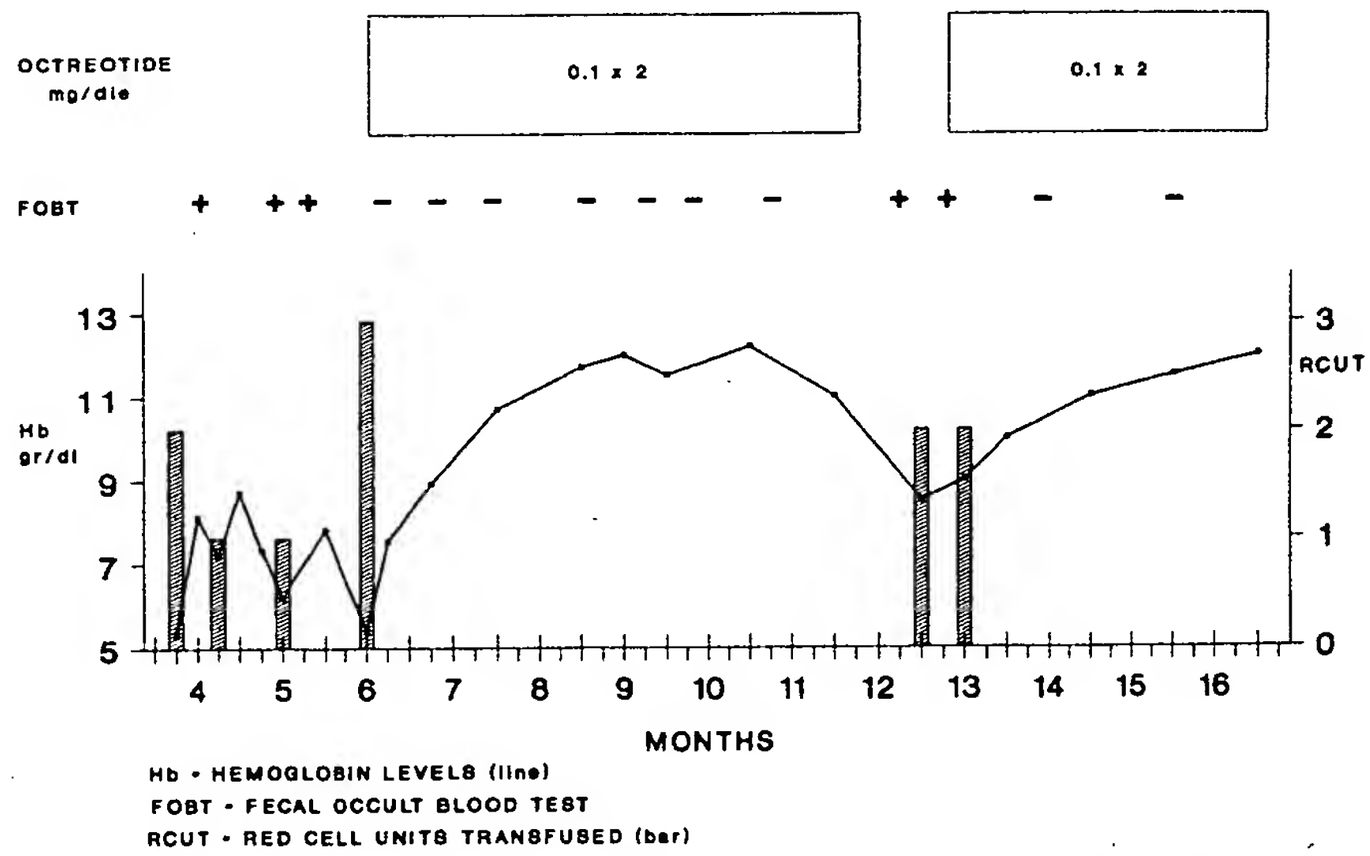

FIG. 2. Hb levels, fecal occult blood test *(FOBT)*, and number of red cell units transfused *(RCUT)* in relation to the treatment of patient II.

was of no avail in case I, and we began with 0.1 mg twice a day in the other cases. The fact that the effect of the drug is dose-dependent, coupled with the rapidity of the response, suggests that it acts mainly by reducing the splanchnic flow, particularly since the suspension attempted in one case, albeit after only 6 months, was quickly followed by recurrence. This in itself, plus persistence of angiodysplasias in the single control jejunoscopy, shows that, whereas bleeding is controlled, the lesions are not reduced. Suspension after a longer period (*e.g.*, in case I) could perhaps be followed by a stable result.

Octreotide was well tolerated. There were no instances of diarrhea, steatorrhea, or changes in glucose metabolism (18). Its renewed effectiveness after suspension should also be noted, and the drug's long-term efficacy seems clear. In case I, for example, it has been administered at the full dose for 2 yr with no apparent loss of effect. The tachyphylaxis and consequent dose augmentation described for other amino acid derivatives do not appear to constitute an impediment to long-term octreotide management.

The conclusion to be drawn, therefore, is that octreotide may be efficacious in both the short- and long-term control of bleeding due to angiodysplasia, although a follow-up jejunoileoscopy showed that lesions do not regress. Further investigation of the drug's performance is obviously required. However, the relative infrequency of bleeding due to angiodysplasia of the small intestine and its difficult diagnosis will make it hard to mount a randomized double-blind trial against other therapies.

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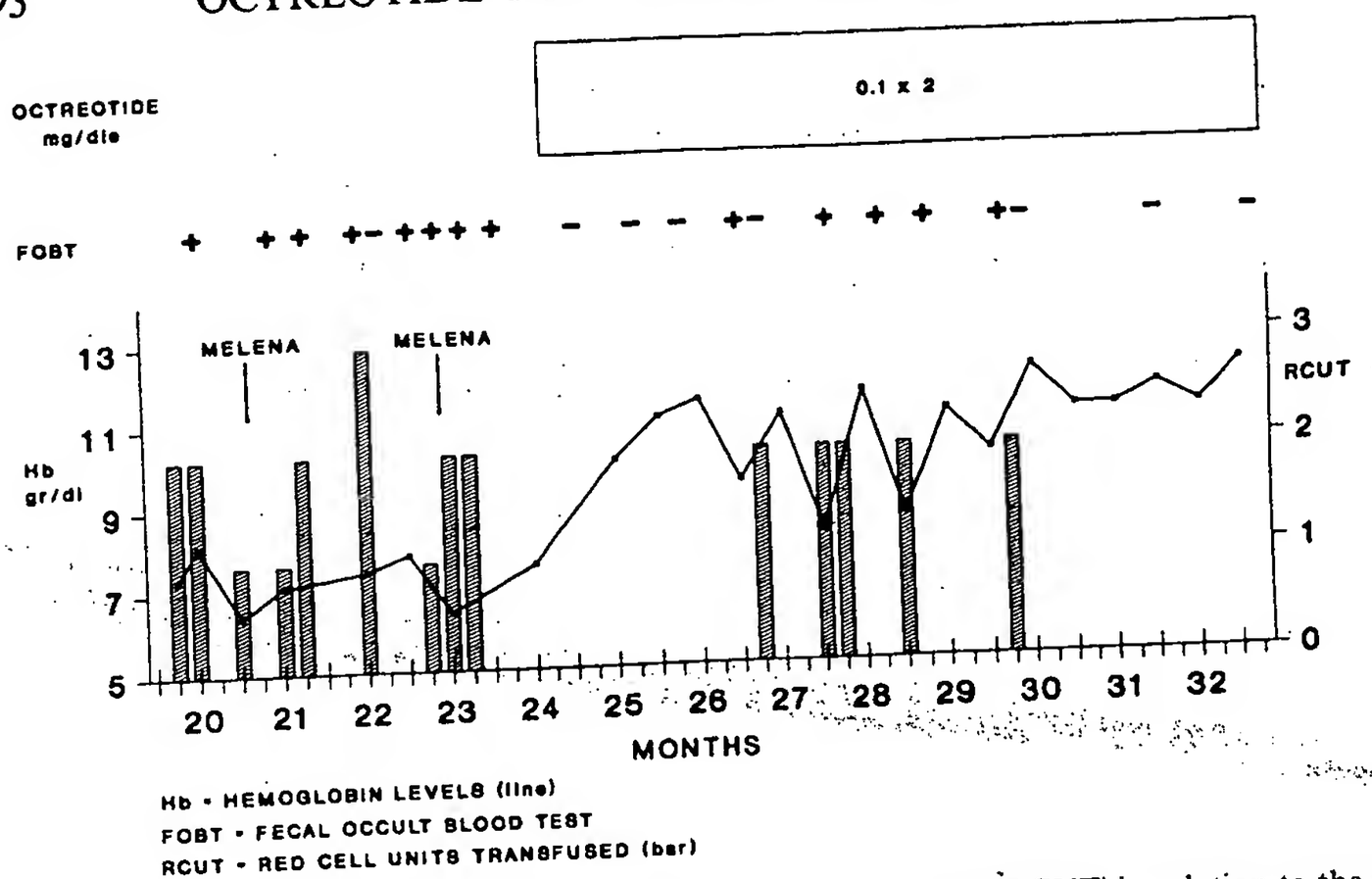

FIG. 3. Hb levels, fecal occult blood test *(FOBT)*, and number of red cell units transfused *(RCUT)* in relation to the treatment of patient III.

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